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First case of human cerebral *Taenia martis* cysticercosis

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Abstract

Taenia martis is a tapeworm affecting mustelids, with rodents serving as intermediate hosts. The larval stage (cysticercus) has before been found only rarely in humans or primates. We hereby describe a case of cerebral *T. martis* cysticercosis in a French immunocompetent patient, confirmed by DNA analyses of biopsy material.

Case report

In January 2012, a 44-year-old woman with no significant medical history except Verneuil's disease was admitted to the Strasbourg University Hospital for right hemiparesis and aphasia. Cerebral magnetic resonance imaging (MRI) revealed fluid attenuated inversion recovery (FLAIR) and diffusion signal abnormalities in a small area of the left temporal lobe cortex, associated with leptomeningeal gadolinium-based enhancement in the depth of the adjacent sulcus (Fig. 1, 2). On examination, the patient was found to have a temperature of 38.5°C. She reported no travel history outside of Europe and presented no immunosuppression. Meningoencephalitis was suspected and the first examination of the cerebrospinal fluid (CSF) revealed lymphocytic pleocytosis, increased protein levels, and normal glucose concentration. Bacterial antigen detection in CSF was negative, as were CSF bacterial and fungal cultures. Acyclovir, cefotaxime, and amoxicillin were initiated. Five days later, a second lumbar puncture revealed 790 leucocytes/mm^3 (70% lymphocytes, 30% eosinophils) and oligoclonal immunoglobulin bands.

Due to the eosinophilia, a complementary serological investigation was performed. Serology was weakly positive (1:60) for *Taenia solium*, using *T. solium* antigens and immunofluorescence, and negative for *Echinococcus granulosus* using Western blot with *Echinococcus* spp. antigens (LDBIO Diagnostics, Lyon, France), *E. multilocularis* using enzyme-linked immunosorbent assay (ELISA) with Em2+ antigens, (Bordier Affinity Products SA, Crissier, Switzerland), *Taenia saginata* using *T. saginata* antigens and immunofluorescence, *Schistosoma mansoni* using ELISA with *S. mansoni* antigens (Bordier Affinity Products SA), *Trichinella spiralis* using ELISA with *T. spiralis* antigens (LDBIO Diagnostics), and *Strongyloides stercoralis* using ELISA with *S. ratti* antigens (Bordier

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Affinity Products SA). Stool examinations were negative for parasites. The patient fully recovered the following week. She was re-admitted in May 2012 after another episode of aphasia. Cerebral MRI was then performed again, displaying a ring-enhancing lesion along with a small enhancing nodule attached to its border, associated with significant perilesional edema, in the same cortical area as that recorded on the first MRI.

Despite MRI revealing no evidence of neoangiogenesis, due to the cerebral blood volume being diminished, there were no clinical features that enabled the distinction from an inflammatory process due to either unknown infection or tumor, such as a glioblastoma or metastatic process. Surgical exeresis of the parasitic mass was performed. The pathological examination demonstrated no signs of a tumoral process, yet revealed a thick-walled parasitic cyst with dense fibrosis and intense mononuclear inflammation. The cyst contained dense fluid consisting of thick bright eosinophilic ribbons of membranous tissue and calcareous corpuscles, characteristic of cestodes. Several punch biopsies of the suspected lesion were carried out by means of laser capture microdissection.

DNA was extracted from the dissected tissues. Polymerase chain reaction (PCR) testing was negative for *Echinococcus granulosus* and *E. multilocularis*, though positive for *Taenia* spp. (1). Fragments of the mitochondrial cytochrome c oxidase subunit 1 (*cox1*), NADH dehydrogenase subunit 1 (*nad1*), and 12S ribosomal ribonucleic acid (rRNA) (*rRNAS*) genes were amplified by means of PCR using primer pairs JB3/JB4.5 (2), JB11/JB12 (3), and Cest3/Cest5 (4), respectively. Both partial sequences of the *cox1* (396bp) and *nad1* (488bp) genes demonstrated 100% homology with published *T. martis* sequences (EU544557 and EU544607). For the rRNA gene, the sequence (263/265bp) demonstrated 99.2% homology with a published *T. martis* sequence (JX415820). Lower sequence identities were also revealed between our specimen and *T. crassiceps* (90 and 82% for *cox1* and *nad1*,

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respectively) or *T. twitchelli* (94 and 86% for *cox1* and *nad1*, respectively). Cerebral cysticercosis diagnosis was thus established based on the presence of *T. martis*. A phylogenetic tree was created using the sequences obtained in this study as well as those of representative *Taenia* species accessed from GenBank (Fig. 3).

Surgical exeresis of the parasitic mass was performed, and the patient was treated with praziquantel (50mg/Kg/day) for 15 days and albendazol (15mg/Kg/day) for 1 month, combined with corticosteroids (1mg/Kg/day). Three years thereafter, no signs of recurrence were observed.

The patient lives in the forested part of the French Vosges region, consisting of a woody mountainous area at medium altitude with temperate climate in eastern France. She has three cats and a dog, with a garden where she grows vegetables, with free access to the nearby forest. Fecal samples collected from her cats and dog were investigated and taeniid eggs were detected in one cat and the dog. The eggs were identified as *Taenia taeniaeformis* (4). *T. martis* was not identified. Fecal samples collected from the house's surroundings, suspected to originate from martens, were also negative for *T. martis*.

Several cestode species are currently known to be human parasites. Some are capable of invading the central nervous system (CNS), namely *Taenia solium* and *Echinococcus granulosus*. Neurocysticercosis caused by *T. crassiceps* or *T. multiceps* is less common, yet should be considered in the differential diagnosis of CNS infections. *T. martis* cysticercosis was recently reported for the very first time in a human eye (5).

T. martis is usually found in adult stages in the small intestines of stone martens. Other carnivores, including mustelids of the *Mustela*, *Meles*, *Lutra* or *Gulo* genera, and, more rarely, canids of the *Canis* and *Vulpes* genera, as well as wild cats, may also act as definitive hosts

(6). Rodents and other small mammals serve as intermediate hosts and harbor the parasite in its larval stage (cysticerci). In rodents, cysticerci are usually found in the pleural and peritoneal cavities. The distribution of *T. martis* ranges from Europe (*T. m. martis* subspecies) to North America and Russia (*T. m. americana*) (6). In Europe, *T. martis* has been observed in martens and rodents in Italy, Germany, The Netherlands, Belgium, Spain, Poland, Belarus, and Switzerland (7-9). Recently, fatal *T. martis* cysticercosis was identified in a Tonkean macaque (*Macaca tonkeana*) in Eastern France near Strasbourg (Alsace region) (10) and in a ring-tailed lemur (*Lemur catta*) in the zoological gardens of Rome, Italy (11). These recent cases are evidence of potential lethal outcomes in monkeys and offer particular epidemiological value as indicators of existing environmental contamination with *T. martis* eggs. So far, the only human case that has been described involved the eye of an immunocompetent woman in Germany. The patient exhibited a subretinal tumor-like structure resembling a cestode larva, which was treated with albendazole and dexamethasone, and the cyst was removed. The patient lived in southwestern Germany on the east side of the Rhine River, just across from the Alsace area where our case occurred, and the consumption of contaminated homegrown vegetables was suspected as causative risk factor (5). In our patient, the *T. martis* cysticerci developed in the brain and, once treated, her clinical evolution turned out favorable. Both cases displayed one unique lesion, potentially due to the non-multiplying nature of *T. martis* larvae, thus limiting the risk of generalization and recurrence (6). Transmission to intermediate hosts occurs *via* the oral route by way of food or water contaminated by fecal matter. In our case, the potential risk factors could have been the consumption of wild berries or garden-grown vegetables contaminated by infected marten or fox feces, as the patient lives near the forest and the intrusion of wild animals into the garden is possible. The involvement of her pet animals could not be excluded either, even though the corresponding fecal examinations were negative at the time of sample collection. It is highly

probable that a natural *T. martis* life cycle existed in the environment of the house, given that small rodents (voles, mice, rats, and squirrels) and carnivores (martens and foxes) were regularly observed in close vicinity. In France, the prevalence of *T. martis* in wildlife remains largely unknown, with only few reports available (12, 13). However, the recent observation of a peritoneal *T. martis* cysticercosis in a Tonkean macaque in the Alsace region indicates that local contaminations of this particular environment with eggs of this tapeworm species may occur.

In summary, we hereby describe the first case of a human cerebral infection with *T. martis*. A treatment comprising praziquantel and albendazole as well as surgical exeresis led to a complete cure. Our study further documents the susceptibility of humans to larval *T. martis* infections. Even though the number of diagnosed cases is low, we cannot rule out the possibility that cases may have been missed in the past due to the absence of molecular analysis. We therefore believe that both *T. martis* and *T. crassiceps* cysticercosis should be added to the differential diagnosis of unusual tumor-like CNS lesions.

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FIGURE LEGENDS

FIG. 1. Axial fluid attenuated inversion recovery (FLAIR) (a, e); axial diffusion (b); apparent diffusion coefficient map (c); axial T1 Spin Echo (SE) after gadolinium injection (d). Mild cortical FLAIR and diffusion hypersignal, with mild restriction of the diffusion coefficient in the left temporal lobe (arrow). Leptomeningeal enhancement after gadolinium administration in the depth of the adjacent sulcus (arrow head). White matter subcortical nonspecific hyperintensities (star)

FIG. 2. Sagittal T1 (a); axial T2 Spin Echo (SE) (b); T2 star-weighted angiography (SWAN) (c); axial (d) and sagittal (e) T1 SE after gadolinium injection; axial diffusion (f); apparent diffusion coefficient map (g); cerebral blood volume map (h). Left temporal cortical annular enhancing lesion (arrow). The border of the lesion is thick and partially spontaneously hyperintense on T1 and hypointense on T2, with T2 SWAN suggesting the presence of hemosiderin or calcium deposits (arrow head). The contrast enhancement is predominant in the inner part of the border (arrow). The center of the lesion appears hyperintense on diffusion-weighted MR imaging, with restriction of the diffusion coefficient suggesting thick content (star). In the center of the lesion, there is a small enhancing nodule attached to the border, hypointense on T2 SWAN (circle). The cerebral blood volume is diminished (h). Significant perilesional edema is revealed

FIG. 3. Neighbor-joining tree based on *Cox1* sequences, showing the phylogenetic relationships between the *Taenia martis* isolated from humans and the other tapeworm

species. Shaded triangle refers to the sequence generated by this study and the Genbank accession numbers of each strain are given in parentheses. (a) to (d) refer to *Taenia martis* isolated from humans, *Myodes glareolus*, *Apodemus sylvaticus*, and *Myodes rufocanus*, respectively. Bootstrap values >70% are included to indicate branch support. Neighbor-joining analysis (NJ) was processed using MEGA V.5.2. software and the branch support was evaluated by means of bootstrap test with 1000 replicates (14)

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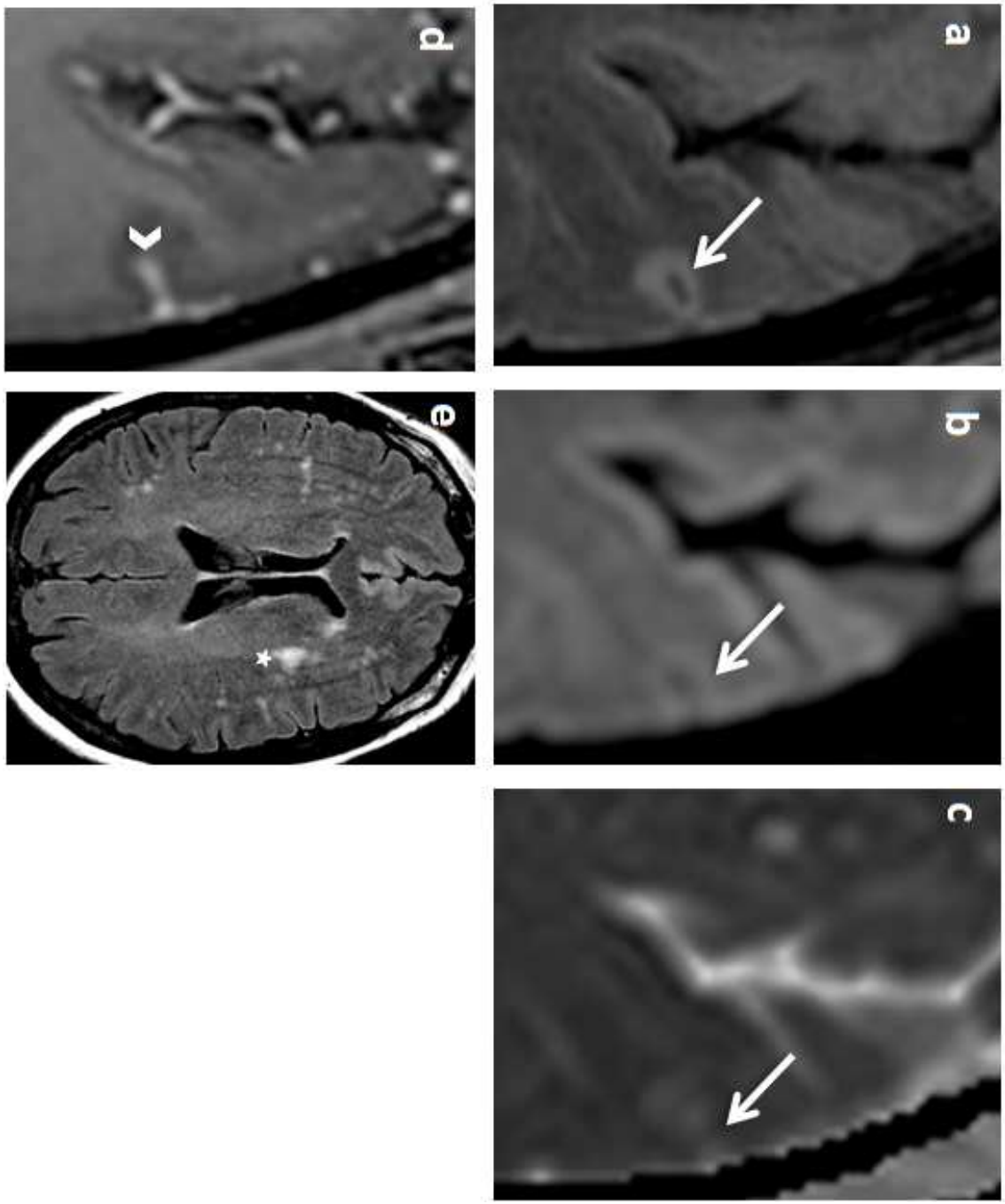
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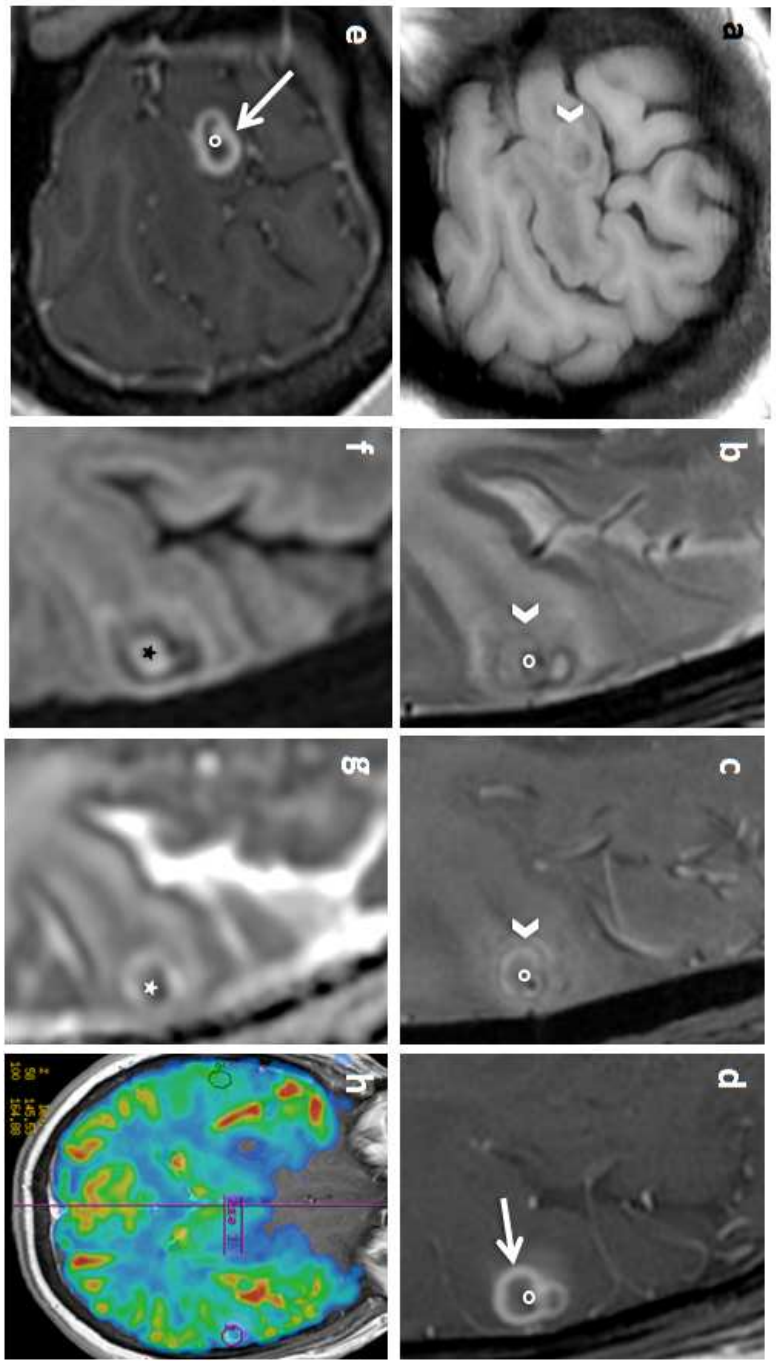
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